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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/410,462	10/01/1999	ANGELICA WILLIAMS		6889

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ONYX PHARMACEUITICALS, INC.
2100 POWELL STREET
12TH FLOOR
EMERYVILLE, CA 94608

EXAMINER	
ANGELL, JON E	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/410,462	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2002*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,22-24 and 26-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20,22-24 and 26-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 October 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 12/15/2004. The change of address has been entered. The amendment filed 7/17/02 is acknowledged. The amendment has been entered. Claims 1 and 6 have been amended; claims 21 and 25 have been cancelled. Claims 1-20, 22-24 and 26-28 are currently pending in the application and are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claim Rejections - 35 USC § 112

The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action.

Claims 1-20 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of reducing the size of a tumor by intratumoral injection of the Ad5 vector disclosed as dl922/947, dl1107 or pm928, does not reasonably provide enablement for the full scope of the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the reasons of record.

Response to Arguments

Applicant's arguments filed 7/17/02 have been fully considered but they are not persuasive.

Applicants argue that page 7; lines 21-22 contemplate modes of administration other than intratumoral injection. Furthermore, applicants state, "Clearly, one of skill in the art would understand that Applicants intend that standard modes of administering adenovirus include systemic administration which could be achieved by a number of means, including intravenous injection." (See page 3 of Applicants' Response). Additionally, Applicants refer to column 17, lines 1-20 of US Patent 5,677,178 (hereafter "the '178 patent") which has been incorporated by reference.

Applicant also argue that page 19, lines 21-22 of the specification shows that intranasal inoculations of dl922/947, which allegedly support the assertion that the claims are enabled. Applicants also direct the Examiner to Examples 3 and 4 which they assert supports in vivo enablement. Furthermore, Applicants assert that the Examiner is requiring that all of the data be from in vivo model system. (See p. 4). Applicants contend that Examples 3 and 4 show that Applicants' methods are enabled for in vivo application of the instant E1A-CR2 Rb mutant viruses as they allegedly show that the viruses show selective in vivo killing in the sense that they will kill dividing cells, cancer cells, but not quiescent normal cells (see p. 5). Applicants also contend that the in vitro system is routinely used to predict in vivo killing properties of adenoviruses, and refer to US Patents 5,998,205 and 5,698,443 as well as two literature references, and assert that the arguments should obviate the enablement rejection.

In response, Applicants arguments and the indicated references have been fully considered but are not persuasive.

With respect to Applicants arguments that the specification has disclosed routes of administration other than intratumoral delivery, it is acknowledged that the specification has disclosed the other routes of administration. The question is whether or not the specification has an enabling disclosure for the full scope of the claims. It is noted that Applicants acknowledge that the claims encompass systemic administration. However, the specification does provide an enabling disclosure for systemic administration or for any other administration other than an administration that would result in the direct delivery of the adenovirus to the tumor cells. Therefore, Applicants arguments that the specification discloses different routes of administration is not persuasive because the specification has not enabled the routes of administration other than direct delivery.

With respect to Applicants arguments regarding the disclosure of the '178 patent, it is acknowledged that the '178 patent discloses the indicated routes of administration. However, the '178 patent does not provide an enabling disclosure for the any route of administration other than direct delivery to the tumor cells. Therefore, Applicants arguments regarding the disclosure of the '178 patent are not persuasive.

With respect to Applicants arguments that page 19, lines 21-22 of the specification shows that intranasal inoculations of dl922/947, it is respectfully pointed out that the specification does disclose in Example 4, (at page 19, lines 21-22) that the dl922/947 virus was administered to a cotton rat by intranasal injection. It is noted that Example 3 shows that intratumoral injection of dl922/947 is effective for killing the tumor cells in a nude mouse model. It is respectfully

pointed out that the rejection has indicated that the claims are enabled to the extent that the claims read on the specific method disclosed in Example 3 (intratumoral injection of Ad5 dl922/947). It is respectfully pointed out that the broad claims are not limited to intratumoral injection of Ad5 dl922/947. Example 4 shows that the dl922/947 virus when delivered by intranasal inoculation has a decreased replication and toxicity in quiescent lung cells compared to wild-type virus. It is noted that Example 4 does not indicate that intranasal inoculation can be used to effectively deliver the adenovirus to any tumor cell in the animal, which is encompassed by the claims. With respect to Applicants' assertion that the Examiner is requiring that all of the data be from in vivo model system, it should be made clear that the Examiner is not requiring all of the data to be in vivo data. The Examiner is requiring the specification provide an enabling disclosure for the full scope encompassed by the claims. It is respectfully pointed out that the claims are very broad and, in their broadest embodiments, encompass treating any tumor in an animal by administering any E1A RB mutant adenovirus by any route of administration, including systemic administration (as acknowledged in Applicants response on page 3). It is noted that Examples 3 and 4 (and all other Examples) have been fully considered as have the US Patents 5,998,205 and 5,698,443 and the two literature references cited. However, the instant specification, the Patents and the cited references do not provide an enabling disclosure for the broad claims.

Therefore, Applicants arguments are not persuasive.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action.

Claims 1-6 remain rejected under 35 U.S.C. 102(e) as being anticipated by Bishoff et al (US Patent 6,080,578), for the reasons of record.

Response to Arguments

Applicant's arguments filed 7/17/02 have been fully considered but they are not persuasive.

Applicants argue that the dividing cells consist of cancer cells and endothelial cells, and assert that Bishoff does not show that the viruses described therein have the killing activity ascribed to the adenoviruses claimed in the instant claims (see page 7). Therefore, Applicants contend that Bishoff does not teach each and every feature of the claims.

In response, Applicants' arguments have been fully considered, but are not persuasive. With respect to Applicants' arguments that claim 1 has been amended to recite that the dividing cells consist of cancer cells and endothelial cells, it is respectfully pointed out that claim 1 specifically recites, "In a cell population comprising dividing and quiescent cells, wherein said dividing cells comprise cancer and endothelial cells, a method... comprising contacting said cell population...with a replication competent adenovirus comprising a mutation in E1A RB family member binding region of said adenovirus...". Given the broadest reasonable interpretation, "a cell population comprising dividing and quiescent cells" encompasses an animal as animals cell populations comprising dividing and quiescent cells. Therefore, given the broadest reasonable

interpretation, the claims encompass a method wherein the mutant adenovirus is "contacted with" an animal comprising dividing cancer and endothelial cells. Bishoff teaches administering treating cancer by administering a mutant adenovirus encompassed by the claims to the cancer cells wherein the cancer cells are in an animal (e.g., see column 10, lines 10-42; column 16, lines 18-67; column 17, lines 1-35; column 18, line 30 through column 19, line 56, etc.). Therefore, Bischoff does teach the limitations of the instant claims.

Therefore, Applicants' arguments are not persuasive.

New Grounds of Rejection

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-24 and 26-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22-24 depend on claim 21. However, claim 21 has been cancelled.

Claims 26-28 depend on claim 25. However, claim 25 has been cancelled.

Therefore, claims 22-24 and 26-28 are indefinite because they depend on cancelled claims.

Rejections Withdrawn

The rejection of claims under 35 USC 112, second paragraph have been withdrawn in view of the amendment to the claims. However, a new grounds of rejection under 35 USC 112, 2nd paragraph has been set forth herein.

The rejections of claims under 35 USC 102(b) have been withdrawn because claim 21 and 25 have been cancelled.

The rejection of claims 21-28 under 35 USC 112, 1st paragraph has been withdrawn as claims 21 and 25 have been cancelled.

The rejection of claims 21and 25 under 35 USC 102(e) has been withdrawn as claims 21 and 25 have been withdraw.

The rejection of claims under 35 USC 103 have been withdrawn in view of the Applicants arguments with respect to the secondary reference(s).

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon Eric Angell, Ph.D.
Art unit 1635

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER